

**REMARKS/ARGUMENTS**

Applicants submit this Reply and Amendment in response to the Examiner's Office action mailed on June 13, 2003 setting a shortened statutory period for response of three months. In the subject Office action, the Examiner rejected claims 12-32 under 35 U.S.C. §103(a) as being unpatentably obvious over the combination of Siedel (US Patent No. 6,013,467) and Weisheit (WO 97/45733). The Examiner also rejected claims 12-32 under the second paragraph of 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Applicants thank the Examiner for his time in the interview held at the Patent Office on August 28, 2003. The interview was very helpful in advancing the prosecution of this application, and applicants have prepared this Reply in accordance with the discussions held during the interview.

**1. Rejection of claims under 35 U.S.C. §103(a)**

Applicants respectfully traverse the rejections under §103. As discussed during the interview, the combination of Siedel and Weisheit cannot properly serve as a basis for rejection under §103 because the combination does not disclose each and every limitation of any pending claim.

All independent claims of the present invention require simultaneously determining a first optical measurement at a main wavelength of  $450 \pm 10$  nm, and a second optical measurement at one or more secondary wavelengths of  $480 \pm 10$  nm,  $546 \pm 10$  nm, and  $575 \pm 10$  nm. These main and secondary wavelengths are critical to the present invention (see last paragraph on p. 6 of the present application as filed). While Weisheit discloses methods in which the secondary wavelengths are greater than 475 nm, *it does not disclose any method in which the main measurement wavelength is  $450 \pm 10$  nm.* The inventors of the present application are familiar with the Weisheit methods, and believe that, while the disclosed methods work well for some enzymatic assays that utilize a main wavelength of 340 nm, they do not work for assays with a different main wavelength, such

as the determination of alkaline phosphatase. Alkaline phosphatase is typically measured at approximately 405-415 nm due to the absorbance spectra of 4-nitrophenol, which is formed as result of the reaction between alkaline phosphatase and the substrate 4-nitrophenyl phosphate. Indeed, review of Weisheit reveals a lack of disclosure of 4-nitrophenyl phosphate, a reagent used in the determination of alkaline phosphatase and required by all pending claims of the present invention. This further highlights the inapplicability of Weisheit to assays for the determination of alkaline phosphatase.

Siedel does not cure this defect of Weisheit. While Siedel states that "[t]he method is particularly preferably carried out with optical measurements in the measurement wavelength ranges of about 380-450 nm and in particular of 400-420 nm or/and 520-590 nm where hemoglobin has its main and secondary absorptions" (column 2, lines 25-29), it does not disclose the combination of the main and secondary wavelengths recited by the pending claims of the present application. Specifically, Siedel does not disclose a main wavelength of  $450 \pm 10$  nm with one or more secondary wavelengths of  $480 \pm 10$  nm,  $546 \pm 10$  nm, and  $575 \pm 10$  nm. This defect of Siedel is highlighted in Example 1, which is directed to a determination of alkaline phosphatase. The method uses 4-nitrophenyl phosphate and measurements at 405 and 700 nm. Example 1 does not describe any alternative main or secondary wavelengths, and Siedel does not provide any further Examples that are directed to the determination of alkaline phosphatase.

Siedel and Weisheit actually teach away from each other, further making the rejection with this combination of references improper. Siedel discloses methods for eliminating hemoglobin interference that utilize peroxidic compounds as bleaching reagents. The addition of a peroxidic compound is critical to the practice of the Siedel methods (see, for example, column 1, lines 42-47). According to Siedel, "[t]he addition of peroxidic compounds leads to a rapid bleaching of the colour caused by the haemoglobin or haemoglobin derivative...." (column 2, lines 6-8). Thus, Siedel teaches the use of an *additional* reagent (peroxidic components) to eliminate interference, as opposed to an alteration of the wavelengths at which measurements are taken. Weisheit, on the other hand, teaches that changing the optical measurement conditions by alteration of a secondary wavelength is suitable to eliminate interference. These two references,

therefore, teach two different approaches to eliminating interference caused by hemoglobin. Because each reference teaches away from the approach followed by the other, one skilled in the art would have no motivation to combine these references to produce the present invention. The Examiner's §103 rejection based on this combination of references is thus improper and should be withdrawn.

**2. Rejection of claims under second paragraph of 35 U.S.C. §112**

Applicants have herein amended independent claims 12, 24, and 28 to more particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the applicants have amended the preamble of each of these claims to recite a method of determining alkaline phosphatase in which interference by hemoglobin is eliminated. These amendments are fully supported by the specification (see, for example, the first paragraph of the specification as filed).

In the rejection, the Examiner asserted that the claimed methods are incomplete because claims 12, 24 and 28 include no method steps that accomplish the preamble. Nevertheless, as now amended, all of the claims recite such a method. Accordingly, the claims fully comply with the second paragraph of section 112, and this rejection should be withdrawn.

Applicants have also herein amended claim 24 to correct a typographical error in the preamble. Specifically, applicants have deleted "4-nitropheny" and replaced it with "4-nitrophenyl". This amendment is made simply to correct a minor typographical error, and does not narrow the scope of protection sought in any manner.


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**CONCLUSION**

In light of the above, Applicants have overcome each and every one of the Examiner's rejections. The application is therefore in condition for allowance on the next Office action. If, however, the Examiner feels that personal communication would facilitate the prosecution of this case, applicants request that the Examiner contact their attorney at the number listed below.

Respectfully submitted,

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